UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,555	02/25/2002	Michael G. Goggins	JHU1700-1	7972

28213 7590 03/15/2005

DLA PIPER RUDNICK GRAY CARY US, LLP
4365 EXECUTIVE DRIVE
SUITE 1100
SAN DIEGO, CA 92121-2133

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,555	GOGGINS ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,10-14,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,12-14,22 and 23* is/are rejected.

7)☒ Claim(s) *10 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Allowability of claims 7-8, 10-14 and 22-23 have been withdrawn in view of the new grounds of rejections discussed below.

New Grounds of Rejections

Specification

2. The amendment filed August 4, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The substitute raw sequence listing and computer readable format of the sequence listing is objected to because the sequences listed as SEQ ID NO: 115 through 118 are not supported by the specification as originally filed.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112: Lack of Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8, 12-14, 22-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting in a subject a cellular proliferative disorder associated with pancreatic cancer or colorectal cancer.....by identifying aberrant methylation regions of the gene or regulatory region, wherein said aberrant methylation comprises hypermethylation and is identified as being different when compared to the same

region of the gene or associated regulatory region in a subject not having said cellular proliferative disorder...., it does not reasonably provide enablement for a method for detecting in a subject a cellular proliferative disorder... by identifying any aberrant methylation.....in any nucleic acid containing specimen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is "undue". These factors include but are not limited to: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented in the specification, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the unpredictability of the art and (8) the breadth of the claims. (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)) *(MPEP 2164.01(a))*.

The claimed invention is drawn to "a method for detecting a cellular proliferative disorder associated with pancreatic cancer or colorectal cancer, comprising: a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of Preproenkephalin A (ppENK) gene; and (b) identifying aberrant methylation of regions of the gene or regulatory region, wherein aberrant methylation is identified as being different when compared to the same regions of the gene or associated regulatory region in a subject not having said cellular proliferative, thereby detecting a cellular

proliferative disorder in the subject". The claims also teach wherein the nucleic acid containing specimen is selected from the group consisting serum, urine, saliva, blood, duodenal fluid, pancreatic fluid, cerebrospinal fluid, pleural fluid, ascites fluid, sputum, stool and biopsy sample. At page 7, the specification teaches that aberrant methylation typically includes hypermethylation as compared with the same region of the gene or regulatory sequences in a subject not having the cellular proliferative disorder. At page 22, paragraph 0055, the specification teaches that "aberrant methylation comprises hypermethylated CpG rich regions (i.e., islands)". The examples beginning at page 38 and detailed description of the invention teach wherein pancreatic cancer cells versus normal pancreata were analyzed to determine hypermethylation state. At page 14, the specification discloses wherein normal gastric, duodenal and colonic mucosa were analyzed to determine hypermethylation state and further at page 21, discuss wherein genes differentially methylated in colorectal cancer were identified. Likewise the examples at pages 38-48 only discuss wherein the claimed method was performed on pancreatic adenocarcinoma cell lines versus normal pancreata. Despite extensive statement in the specification that the method comprises identifying "aberrant methylation" in numerous tissue types and sample, there is no enabling disclosure wherein hypomethylation associated with a cellular proliferative disorder in any tissue type or nucleic acid containing specimen sample associated with pancreatic cancer or colorectal cancer is identified. Likewise, there is no enabling disclosure that suggest that the identification of hypomethylation in the ppENK gene is indicative of detecting in a subject a cellular proliferative disorder associated with pancreatic cancer or colorectal cancer. The specification does not provide any information to enable one of ordinary skill in the art to use the claimed invention to detect a cellular proliferative disorder

associated with pancreatic cancer or colorectal cancer by determining any methylation state of ppENK gene, except for hypermethylation or in any nucleic acid containing specimen, except for those associated with pancreatic cancer and colorectal cancer. The specification does not provide any reasonable method for detecting any aberrant methylation of the ppENK gene that bears a reasonable correlation to the entire scope of the claims. The examples beginning at page 38 lack information and guidance as to how determination of any aberrant methylation, such as hypomethylation in the gene, ppENK, is associated with or is relevant to the detection of a cellular proliferative disorder associated with pancreatic cancer or colorectal cancer. In order to utilize the invention commensurate fully in scope would require undue experimentation to the practitioner. Nowhere in the examples does the specification disclose, relate or correlate the hypomethylation state of the gene, ppENK, to the detection of any cellular proliferative disorder. Merely making reference to the method being applicable to any aberrant methylation in the ppENK gene and any specimen-types as indicated in claim 14 does not enable the practitioner to reproduce the results as claimed for the broad scope of the claimed invention. Thus, the full scope of the claimed invention is not reproducible due to the lack of guidance provided in the specification. As noted, the specification does properly disclose a method of detecting a cellular proliferative disorder that bears a reasonable correlation to the entire scope of the claims. As to the level of predictability and unpredictability in the art, the level of skill in the art at the time of the invention is very high. However, the level of unpredictability in molecular biology is also high. Although certain techniques useful in the claimed invention were known in the art, the art does not teach a method of detecting a cellular proliferative disorder by determining the

hypomethylation state of ppENK gene in any nucleic acid-containing specimen as described in the claimed invention.

For all of the forgoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention. To overcome the rejection above, it is suggested amending the claim 7 to encompass the limitations recited in claim 10. It is also suggested amending the claim 14 to recite only those nucleic acid specimens related to colonic cancer and pancreatic cancer.

Claim Rejections - 35 USC § 112: New Matter

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim 22 is drawn to a method of claim 12, wherein the primers pairs are selected from SEQ ID NOS: 115, SEQ ID NO: 116 and SEQ ID NO: 117, SEQ ID NO: 1118. The sequences recited as SEQ ID NOS: 115-118 are not supported by the specification as originally filed. Nowhere in the specification is there a teaching of the sequences recited as SEQ ID NOS: 115-118. Applicant does not provide any cited support for the newly added sequences and only state in remarks filed on August 4, 2003 that these sequences were derived from SEQ ID NO: 8. However and alignment and search of SEQ ID NO: 8 show very little to no sequence homology

between the sequence recited in SEQ ID NO: 8 and the newly added sequences SEQ ID NOS: 115-118. There is no evidence provided anywhere in the specification or raw sequence listing as originally filed to suggest to one that these sequences recited in SEQ ID NOS: 115-118 were originally present. Therefore, the specification would not have suggested to the skilled artisan that the applicant was in possession of the claimed invention as of the filing date of the application.

Conclusion

6. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600